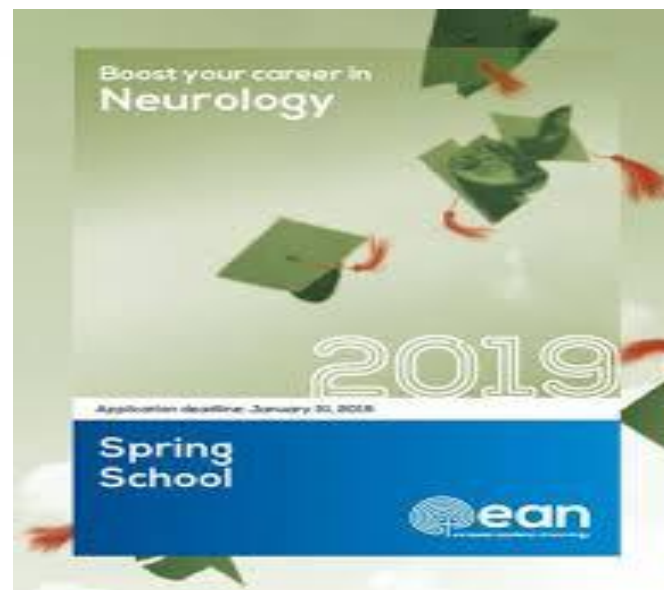




neurology clinic
clinical center of serbia



UNIVERSITY OF BELGRADE
SCHOOL OF MEDICINE

Update on cerebral non-atherosclerotic vasculopathies

Milija D. Mijajlović

Non-atherosclerotic vasculopathies

Athero-
sclerosis

Cardio-
embolism

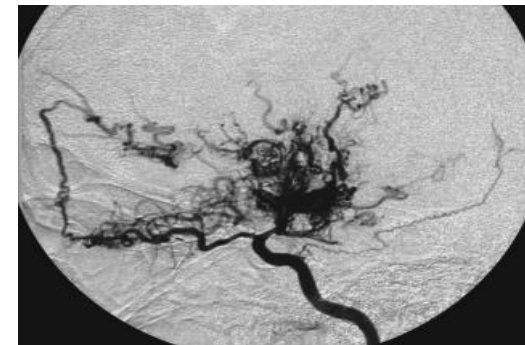
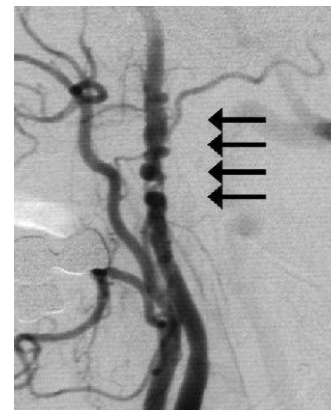
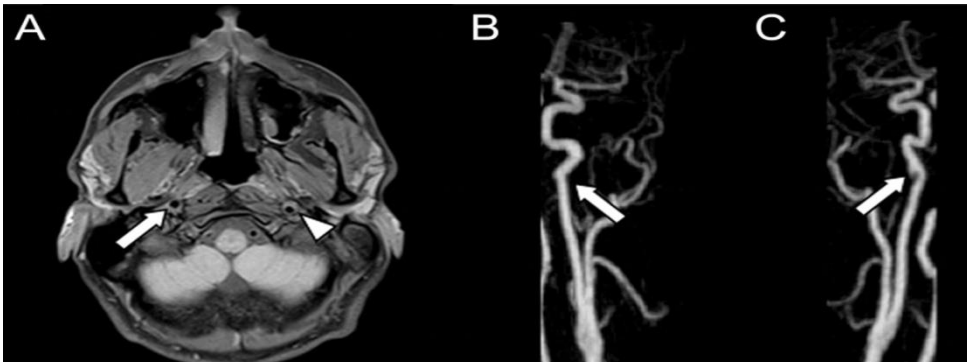
Small artery
disease

Other causes

Unspecified
causes

- Arterial dissections
- Arteritis (GCA, Takayasu)
- Fibromuscular dysplasia
- Moya-moya disease

- About **1-2.5%** of all strokes
- 25% stroke in children and young adults
- The most common cause of stroke under 50 years



Cervical Artery Dissection (CAD)

Arteries have three layers:

- intima, media, adventitia

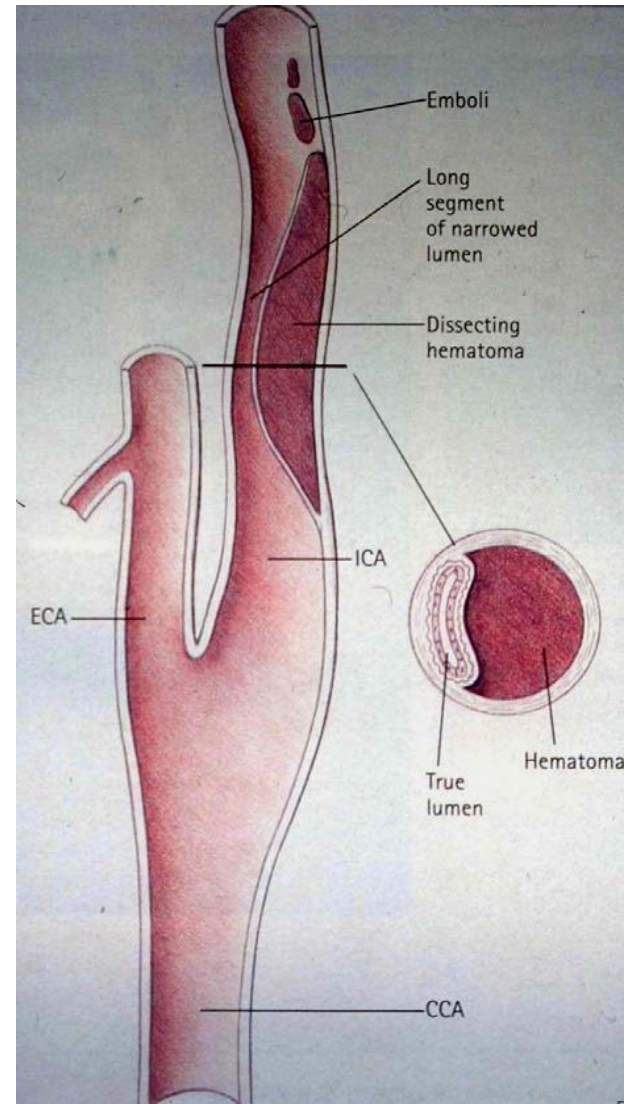
Dissection = a tear in the media or rupture of the vasa vasorum that causes bleeding within the arterial wall

Blood then “dissects” through the arterial wall longitudinally

- subadventitial
- subintimal

Associated risks:

- compressive occlusion of artery
- perforation into the lumen
- thrombogenesis



Introduction

- Common sites: ICA 2-3cm distal to the bifurcation and at the skull base
- VA: V3 between the C1 and C2 of the atlas loop before entering the dura, Proximal VA dissection is rare

Symptoms

- Unusual and unilateral sharp neck pain:
ICA: antero-lateral neck radiating to the mandible and ear (20-40%), VA: dorsal neck (50%)
- Pulsatile tinnitus (10-15%, more common in ICA dissection)
- Transient monocular blindness (10 -15% in ICA dissection)
- TIA (10-20%)
- Metallic taste

Signs

- Asymptomatic
- Horner's syndrome (40-50% in ICA; VA dissection: 20 % central Horner's)
- Cranial nerve deficit (ICA dissection: 5-12%, III-XII)
- Lower cranial deficits are more common in VA dissection
- Cerebral infarction
- SAH

Epidemiology

- ❑ CAD accounts for less than 2% of all ischemic strokes
- ❑ But common cause of stroke in the young <45 years, accounting for 8-25% of all cases
- ❑ Annual incidence rate 2.5-2.9/100.000
- ❑ Overall prevalence underestimated since a large number may remain asymptomatic
- ❑ Slight male preponderance (53-57%)
- ❑ Reported rates tend to be higher in countries where access to health care professionals is higher

Underlying Defects/Risk factors

- **Ultrastructural aberrations** of dermal collagen fibrils and elastic fibers in ~50% of patients with spontaneous CADs=molecular defect in the biosynthesis of the extracellular matrix.
- **Seasonal variability**, particularly increased CAD occurring more often in autumn or winter=increased occurrence of infection or weather-related changes in blood pressure.
- Possible association between an elevated C-reactive protein and dissection=**inflammation** may play a role?
- Mild **mechanical stress**: coughing, head turning, sport activity
- Chiropractic maneuvers or direct **trauma**
- **FMD** up to 15% of patients
- Heritable **connective tissue disease** : EDS, Marfan's sy
- Migraine with aura and hyperhomocysteinaemia
- **Iatrogenic**
- **Traditional risk factors are less commonly associated with CAD**

Imaging Modalities

- Carotid Doppler (poor sensitivity in CAD and mild stenosis)
- MRI and MR Angiography
- CT and CT Angiography
- Digital Subtraction Angiogram carries a small <1% risk of serious complications(stroke)

* MRI studies have the advantage of demonstrating the dissection, false lumen thrombus as well as the ischemic stroke not usually seen early on the CT

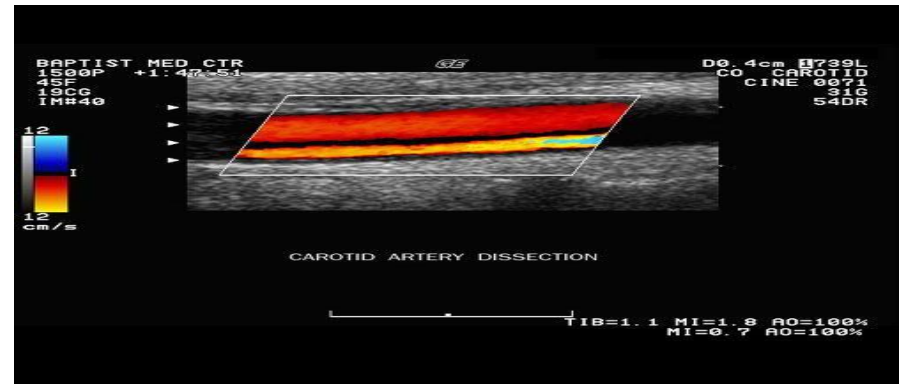
• It is recommended that radiological vascular non-invasive studies should be repeated as occluded CAD often recanalize even spontaneously

Color Duplex Ultrasound

Appearance in dissection: thickened, hypoechoic vessel wall (intramural haematoma).

Flow velocity diminished.

Intimal flap visible in < 33%.



PROS:

- Noninvasive, quick, no contrast required
- 95-96% sensitivity in high-grade stenosis (e.g. patients with cerebral ischemia)
- Offers a dynamic view of the vessel, similar to angiography

CONS:

- Mandible frequently impedes visualization
- Decreased sensitivity in cases of low-grade stenosis (71%)
- Flow velocity measurements may be confounded by comorbid conditions (e.g. AVM, vasospasm)

CT Angiography

High-resolution, high-contrast images.

Often combined with non-contrast CT to evaluate for intracranial hemorrhage.

Appearance in dissection: Intramural thrombus/haematoma appears as low attenuation crescent; diameter of the ICA usually increased.

May see dissection flap \pm double lumen.

PROS:

- Noninvasive
- Images often in close agreement with those of conventional angiography
- Allows 3D reconstructions for better visualization of dissections.

CONS:

- Low attenuation crescent non-specific for intramural hematoma (e.g. can also be seen in atheromatous plaque)
- Less favorable option for patients with renal insufficiency/failure

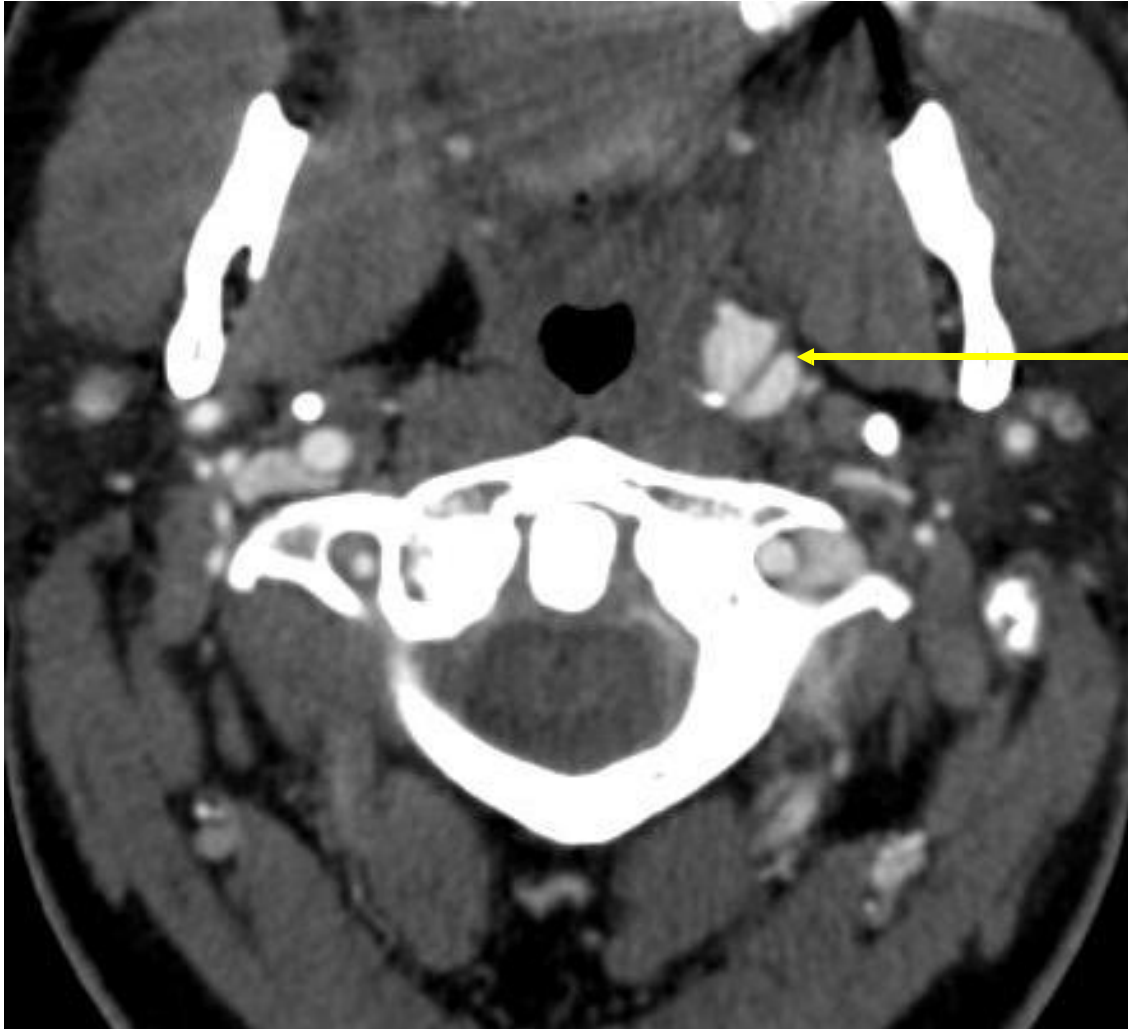
“String Sign”



Marked intraluminal narrowing creates a “string-like” appearance in the area of dissection

Coronal Curved Reformat Head/Neck CTA

ICA Dissection with True and False Lumina on CTA



Dissected ICA
with true and
false lumina

Axial Head/Neck CTA

MRI/MRA

Wide variety of MR imaging paradigms allows for multiple views of dissection with differing enhancement.

On T1-weighted imaging, blood appears as hyperintense, due to paramagnetic properties of hemoglobin breakdown products.

PROS:

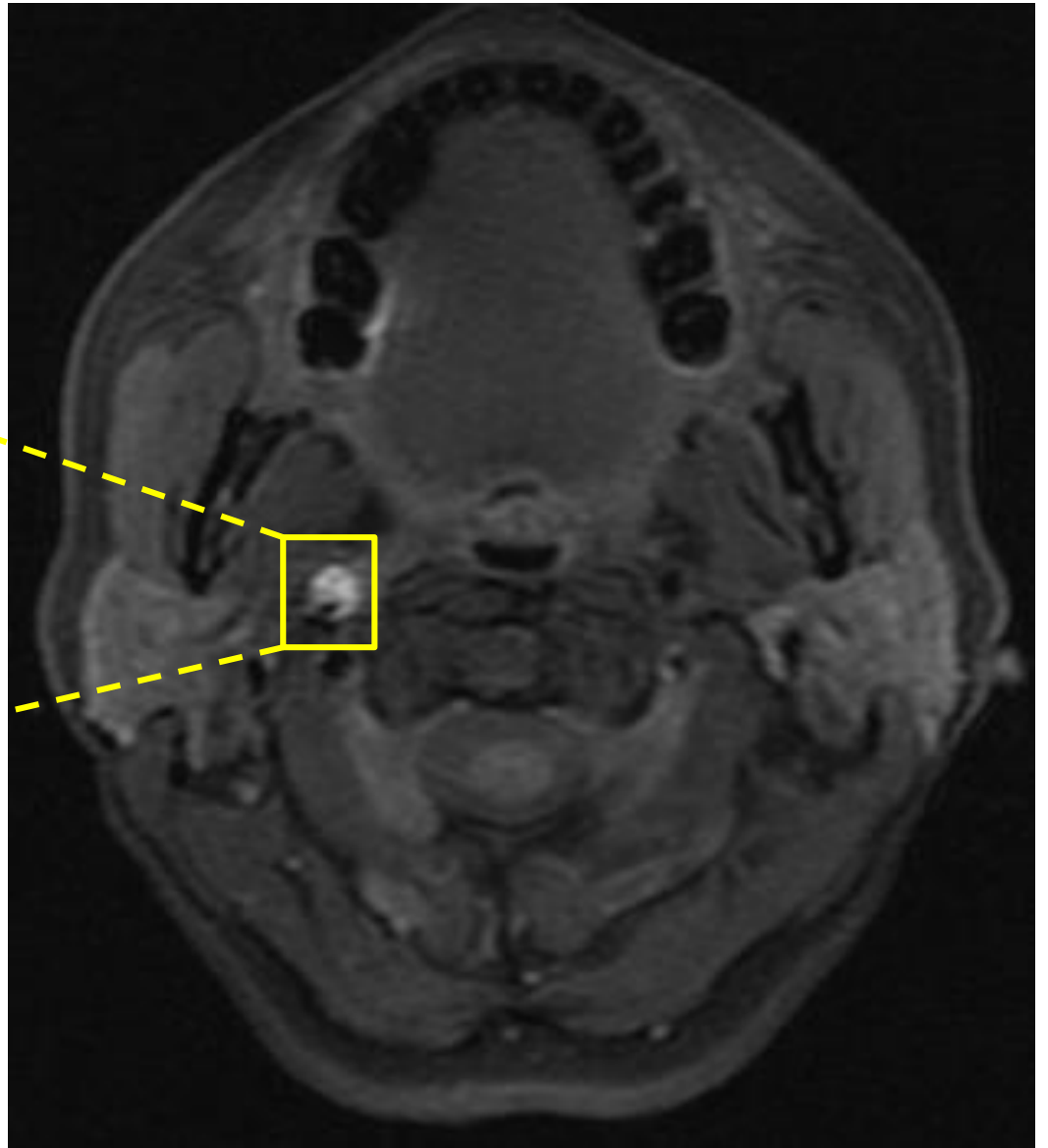
- Hyperintensity of blood allows distinction from plaque and other soft tissue densities
- Excellent sensitivity (95%) and specificity (99%) for ICA dissection

CONS:

- Not as useful for early diagnosis (blood originally appears isointense, then becomes hyperintense as it breaks down over 2-3 days)
- Scans have lengthy acquisition times, require potentially toxic contrast

T1-weighted MRI

Hyperintense
intramural blood
products



Digital Subtraction Angiography

Commonly regarded as the “gold standard”

Typical signs of dissection include: “string sign,” “string and pearl sign” (focal narrowing with distal dilatation), “flame sign” (tapered occlusion sparing carotid bulb), occlusion, and/or pseudoaneurysm.

Pathognomonic signs (double lumen, intimal flap) are rarely observed.

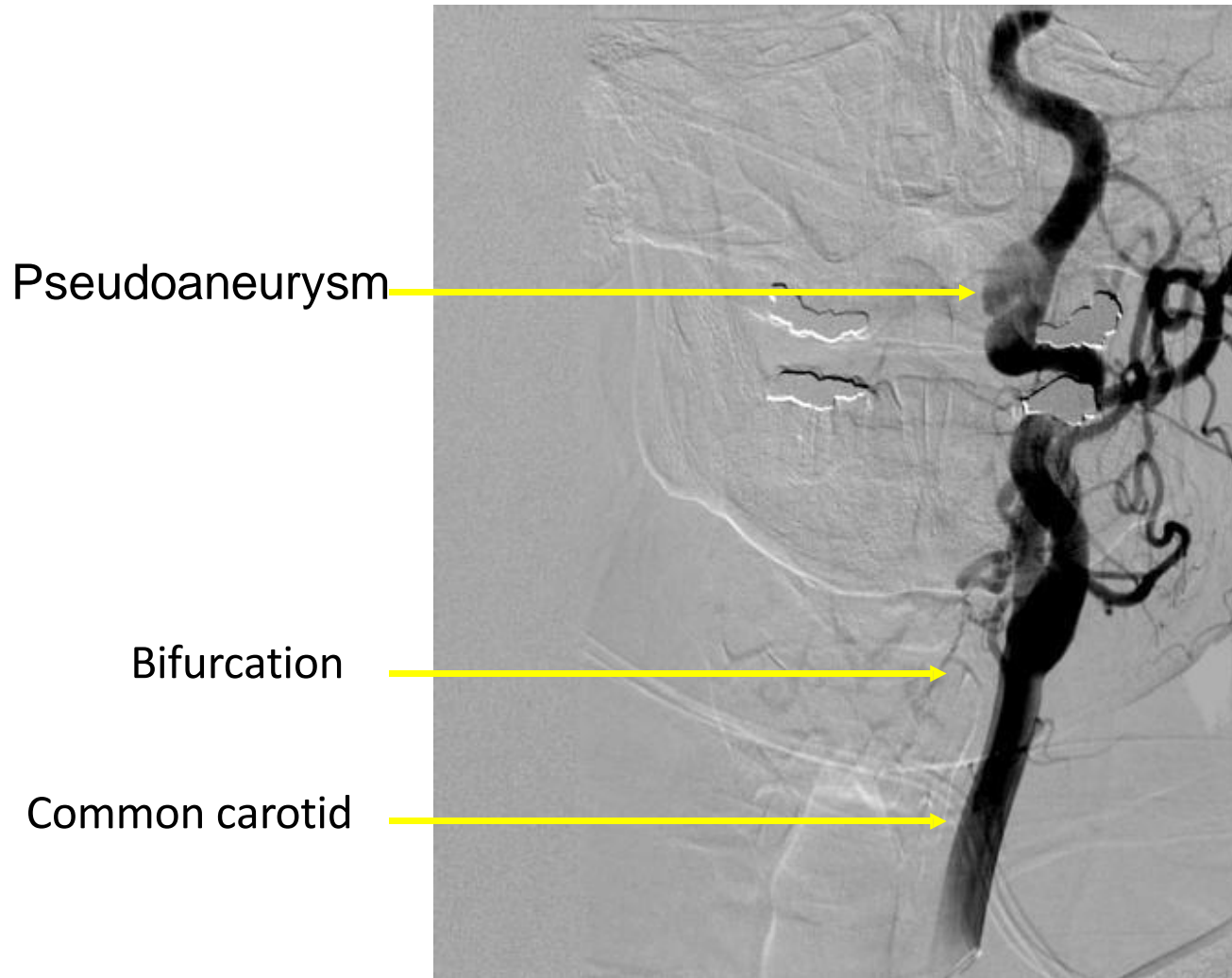
PROS:

- Can observe vessel in real time, obtain information about flow velocity, reconstitution of luminal flow
- Consistent image quality (MR and CT can be easily degraded by artifact)

CONS:

- Does not provide detailed information about the arterial wall (thickness, presence of hematoma)
- Expensive procedure, lengthy
- Risks associated with procedure: hematoma, perforation, renal failure, etc.

Chronic ICA Dissection with Pseudoaneurysm



Sagittal Digital Subtraction Angiography

Recommendations from the ESO- Karolinska Stroke Update Conference, 2016

What is the best method to diagnose CAD?

Contrast enhanced magnetic resonance imaging (MRI) angiography (MRA) and MRI with T1-fat suppression sequences is the recommended imaging modality to diagnose extra- and intracranial CAD.

When not available computed tomography (CT) and CT angiography (CTA) might be alternatives (Grade C).

Treatment

Diversity of treatment options reflects the large heterogeneity of CAD, linked to the association of several crucial factors:

1. Diverse clinical presentation
2. Arterial involvement, which may be single or multiple, extracranial, far more frequently than intracranial, and in the carotid territory more frequently than in the vertebrobasilar territory
3. Morphological status of the artery, which is highly variable, with a lumen that can be normal, stenosed, occluded, enlarged by a dissecting aneurysm or even ruptured, and
4. Delay from symptom onset to stroke, which is crucial in such a dynamic condition in which the dissected artery can rapidly reopen or remain occluded

Acute Therapy - AIS due to CAD

Treatment includes:

- Reopening of the artery in the first few hours when feasible and by the most appropriate method on a case-by-case basis
- Antithrombotic treatment: aspirin or heparin according to the best clinical judgment
- Decompressive surgery in a few selected cases, and
- Stroke unit care with the usual general medical treatment including bed rest if TCD shows signs of hemodynamic compromise.

Recommendations from the ESO- Karolinska Stroke Update Conference, 2016

Acute stroke in the setting of CAD: Is thrombolysis safe?

Acute ischaemic stroke patients with suspected or confirmed **extracranial** CAD should not be excluded from intravenous or intra-arterial thrombolysis or mechanical thrombectomy (grade C).

Recommendations from the ESO- Karolinska Stroke Update Conference, 2016

Is there a role for angioplasty and stenting?

Angioplasty and stenting may be considered in CAD patients with recurrent ischaemic symptoms despite antithrombotic treatment (Grade C).

Impact of Emergent Cervical Carotid Stenting in Tandem Occlusion Strokes Treated by Thrombectomy: A Review of the TITAN Collaboration.

Zhu F, Bracard S, Anxionnat R, Derelle AL, Tonnelet R, Liao L, Mione G, Humbertjean L, Lacour JC, Hossu G, Anadani M, Richard S, Gory B.

Introduction: The TITAN (Thrombectomy in TANdem occlusions) registry was a result of a collaborative effort to identify the best therapeutic approach for acute ischemic stroke due to tandem lesion.

Methods: The TITAN registry included acute ischemic stroke patients with tandem lesions (proximal intracranial occlusion and cervical carotid artery occlusion or stenosis >90%) who were treated with thrombectomy with or without carotid artery stenting.

Results: Prior intravenous thrombolysis and emergent cervical carotid stenting were associated with higher reperfusion (mTICI 2b-3 and mTICI 3) rates at the end of the intervention. Poor outcome did not occur more frequently after stenting than after conservative treatment of the cervical carotid lesion. Emergent carotid stenting with antithrombotic agents and intracranial thrombectomy yielded higher reperfusion rate and good outcome (90 day mRS 0-2) compared to other strategies (carotid artery stenting and thrombectomy without antithrombotic, angioplasty and thrombectomy, or thrombectomy alone). **Etiology of carotid artery lesion (atherosclerosis vs. dissection)** did not emerge as predictor of outcome or recanalization.

Conclusion: Emergent stenting of the cervical carotid lesion with antithrombotic agents in conjunction to thrombectomy appears to be the best treatment strategy for acute ischemic strokes with tandem lesions.

Forty-six studies (n=914) were included in the review; these included one prospective and 45 retrospective studies (no RTCs were identified).

Anticoagulation versus antiplatelet therapy:

There were no significant differences between groups for death (RD 0, 95% CI -0.04 to 0.05; 34 trials), stroke (RD -0.01, 95% CI -0.06 to 0.04; 34 trials), combined TIA and stroke (RD 0.05, 95% CI -0.01 to 0.11; 33 trials), and stroke or death (RD -0.02, 95% CI -0.07 to 0.3; 34 trials).

There was no significant statistical heterogeneity between the studies for any of the outcomes.

Antiplatelet treatment compared with anticoagulation treatment for cervical artery dissection (CADISS): a randomised trial



The CADISS trial investigators*

- CADISS first RCT providing evidence for this clinical question
- Recurrent stroke rate in dissection was extremely low (1.6% at 3 months, 4/250) and there was no difference between anticoagulation and antiplatelet therapy (based on very few endpoints)
- Either approach is reasonable but antiplatelets are easier
- All recurrent strokes were ipsilateral and all in those presenting with initial stroke (2.1% at 3 months, 4/194) - none seen in those presenting with exclusively local symptoms
- Central imaging review failed to confirm dissection in 52 (20%) of patients, suggesting radiographic criteria are not always applied correctly in routine clinical practice
- Randomisation 7 days (early strokes missed?)

FURTHER STUDIES ARE NEEDED

Recommendations from the ESO-Karolinska Stroke Update Conference, 2016

Should we use anticoagulants or antiplatelet drugs to prevent stroke in CAD?

For extracranial CAD:

- a. Antithrombotic treatment is strongly recommended (Grade C).
- b. There is no evidence of any difference between antiplatelets and anticoagulants (heparin followed by warfarin) (Grade B).

For intracranial dissection in the absence of SAH, antiplatelet drugs are recommended (Grade C).

For some patients, mainly those with isolated local symptoms and a normal arterial lumen or a stenosis below 50%, who seem to have a very low risk of ischemic stroke, aspirin on an outpatient basis may be sufficient.

For patients with local signs and/or TIA with a stenosis >50% or occlusion, who are known to have a higher risk of cerebral infarction, stroke unit care and antithrombotic treatment are required and bed rest may be added if there are TCD signs of hemodynamic risk.

Anticoagulants are given – provided there are no contraindications, such as a large infarct – in the rare cases with intraluminal thrombus, low middle cerebral artery (MCA) flow, pseudoaneurysm or recurrence of ischemic events despite aspirin, if endovascular treatment is not feasible.

Recommendations from the ESO- Karolinska Stroke Update Conference, 2016

What is the optimal duration of medical treatment?

Antithrombotic treatment is recommended for at least 6 -12 months

In patients in whom full recanalisation of the dissected artery has occurred and there have been no recurrent symptoms stopping antithrombotic treatment may be considered.

In case of a residual dissecting aneurysm or stenosis, long-term antiplatelet treatment is recommended (Grade C).

DOACs in patients with CAD

A recent single-center retrospective study provides evidence that vascular neurologists at a major academic centers continue to use anticoagulants and have also begun to use DOACs in this setting despite the absence of randomized clinical trial data to support this approach.

In 149 included CAD patients:

- The rate of stroke was similar in patients treated with DOACs (comprising 26.2% of patients), warfarin (comprising 47%), and antiplatelet agents (comprising 26.8%).
- More major hemorrhagic events occurred in the warfarin group (11.4%) compared with the DOAC (0.0%) and antiplatelet (2.5%) groups ($p = 0.034$).
- These data must be interpreted with caution because there was nonrandom allocation of treatment and the numbers are small.
- Nonetheless, patients with cervical artery dissection may constitute a group of patients in which NOACs may prove useful.

Treatment of intracranial CAD

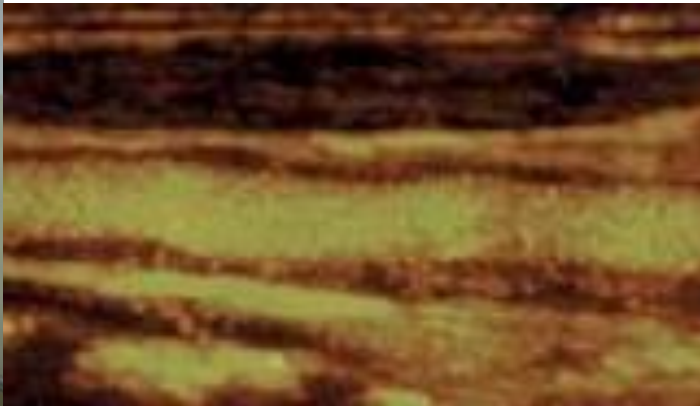
- ❑ Treatment of intracranial artery dissections is empirical in the absence of data from randomized controlled trials.
- ❑ Most patients with SAH undergo surgical or endovascular treatment to prevent rebleeding.
- ❑ Patients with intracranial artery dissection and cerebral ischaemia are treated with antithrombotics.

Outcomes

- Good outcomes with Modified Rankin Scale (mRS) of 0-2, are seen in 70-92% cases
- **Predictors of favorable outcome:**
 - ✓ Recanalization
 - ✓ Lesser initial stroke severity
- **Predictors of poor outcome:**
 - ✓ Bilateral VA dissection
 - ✓ Persistent arterial occlusion
 - ✓ ICA dissection
 - ✓ Older age
- **Predictors of recurrence:**
 - ✓ Family history
 - ✓ FMD
 - ✓ Multiple CADs at initial presentation

Vasculitis of large arteries

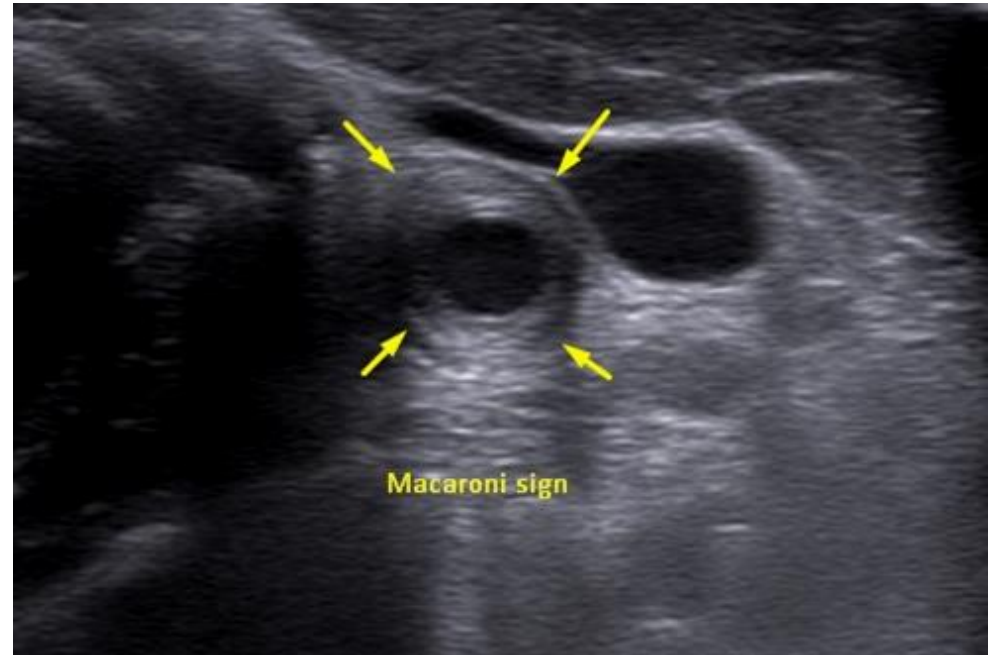
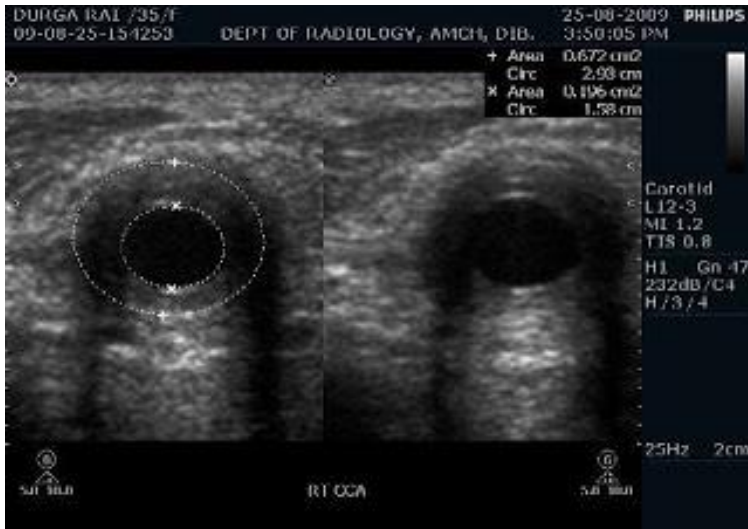
- ❑ The thickening of the wall of the large arteries with inflammatory material
- ❑ Bilateral lesions



Takayasu vasculitis (pulseless disease)

- ❑ <50 years, F: M 9: 1
- ❑ Idiopathic chronic granulomatous panarteritis of aorta and its main branches: common carotid artery, subclavia, thoracic and abdominal aorta
- ❑ Transmural inflammation
- ❑ The most commonly symmetrical bilateral carotid arteries (ACC) and Aa. subclavia (left more often, steal syndrome), collaterals via ACE and especially upper thyroid artery with retrograde flow towards ACI

Macaroni-sign (ACC)



Wall thickness is "mid-echogenic"

False-positive or pseudo-halo:

- If B-gain and color-gain are too low
- If PRF is high
- Inadequate angle of insonation

Takayasu vasculitis - disease monitoring

- Early inflammatory and late occlusive phase of the disease
- Circumference concentric homogeneous thickening of intima-media complex >2 mm, perivascular / periadventic halo, loss of trilaminar thickened IMT - **ACTIVE DISEASE**
- Increasing wall echogenicity supports the reduction of the inflammatory process.
- IMT on ACC > 0.8 mm with a sensitivity of 82% and a specificity of 60-70% speaks in favor of an active disease
- Reduction of the blood vessel diameter, improperly inhomogeneous thickening of the vessel wall, stenosis and occlusion - **CHRONIC DISEASE.**
- Possibility to differentiate the activity of the disease by ultrasound: sensitivity 82% but specificity only 60%

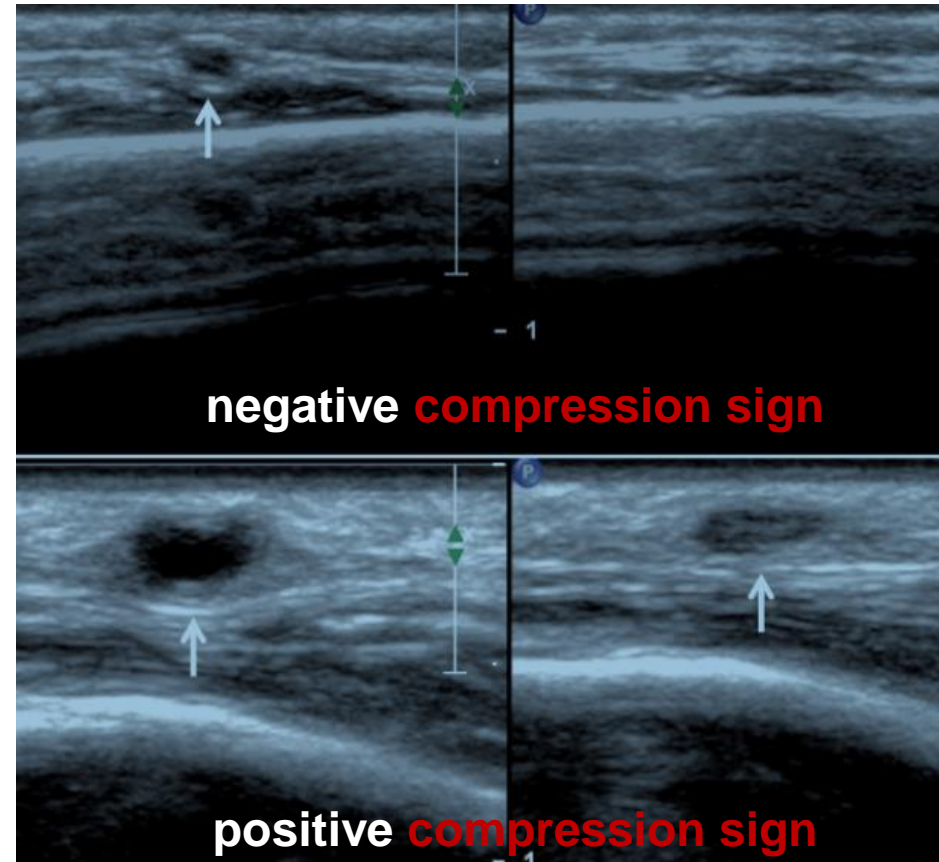
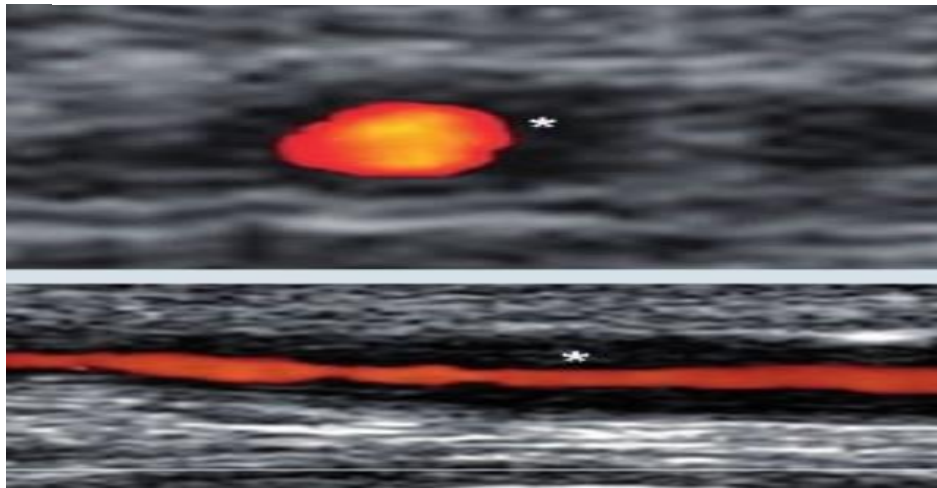
CVS	<p>↓/- pulses (84–96%) -claudication & BP Diff ,Bruits (80–94%) -carotids, subcl & abd vess.</p> <p>HTN- (33–83%) –McC RAS (28–75%), ↓Ao capacitance, atyp CoA, baroreceptor reactivity</p> <p>CHF-(28%) - HTN, AR, DCM-5%</p> <p>AR-(7-24%) Ao root dil > valve inv, annuloaortic ectasia</p> <p>Coronary & vascular involvement</p>
CNS	Cerebral ischemia 2 ^o to obliterative arteritis, seizures etc
RENAL	RAS & Ischemic Nephropathy
SKIN	Erythema nodosum, Raynauds disease, leg& hand ulcers
PULMONARY	<p>15-27%, stenosis/ occlusion of lobar/segmental pul art</p> <p>UL>LL, R>L—INDIA (Panja et al 1997)</p>

ULTRASONOGRAPHY OF TEMPORAL ARTERIES

Role of ultrasound in the understanding and management of vasculitis

Wolfgang A. Schmidt

Ther Adv Musculoskel Dis
2014, Vol. 6(2) 39–47
DOI: 10.1177/
1759720X13512256
© The Author(s), 2013.
Reprints and permissions:
[http://www.sagepub.co.uk/
journalsPermissions.nav](http://www.sagepub.co.uk/journalsPermissions.nav)



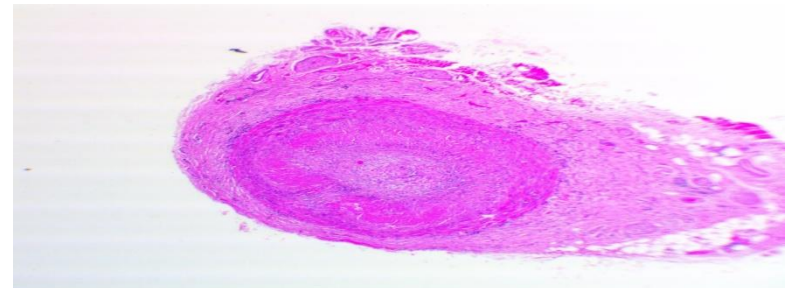
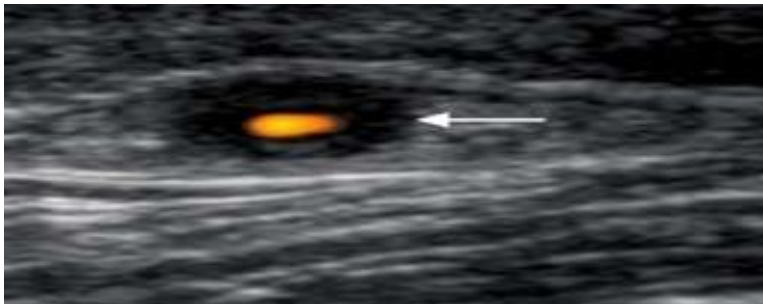
- ❑ The **sensitivity** and **specificity** of the halo sign are **79%** and **82%**, respectively
- ❑ Bilateral halo sign increase sensitivity to **over 95%**
- ❑ The **sensitivity** and **specificity** of biopsy are **55%** and **94%**, respectively

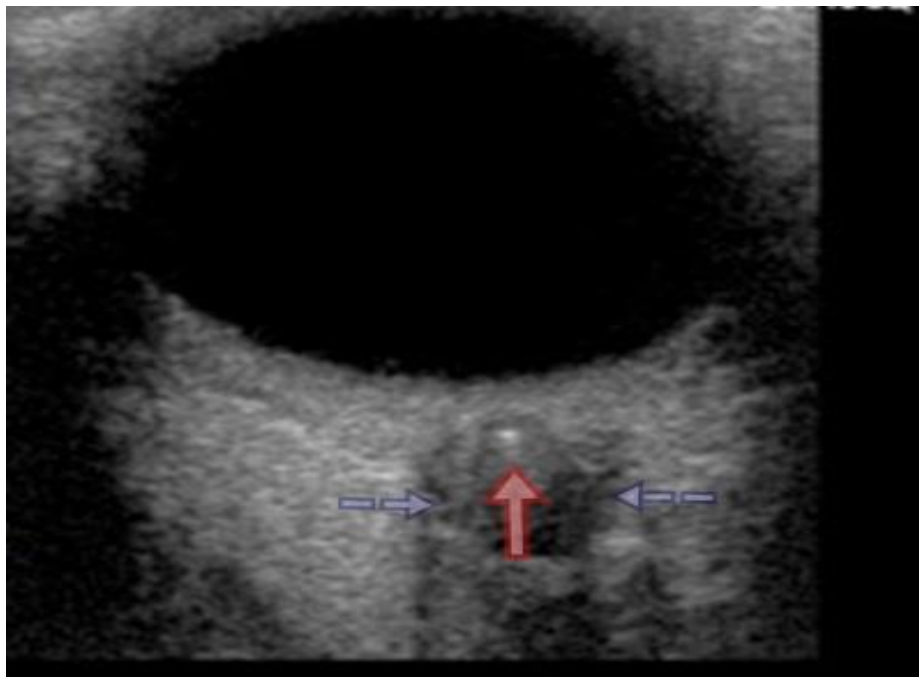
Stenosis and occlusion

- Absent flow in the temporal artery is considered to be an **occlusion** of the artery
- Segmental increase of blood flow velocity with wave forms demonstrating turbulence were classified as **stenosis**
- Similar to halo and compression sign, **stenosis** or **occlusion** are an almost equally sensitive markers for Giant Cell Arteritis compared with biopsy

Duplex vs. Biopsy:

- Temporal artery biopsy could be reserved only for situations where the duplex result is inconsistent with the clinical picture, and the biopsy result, if different from the duplex result, might influence the treatment decision





**Ischemic optic neuropathy
(sudden monocular blindness)**



**RETROBULBAR HYPERECHOGENIC
"SPOT SIGN"**

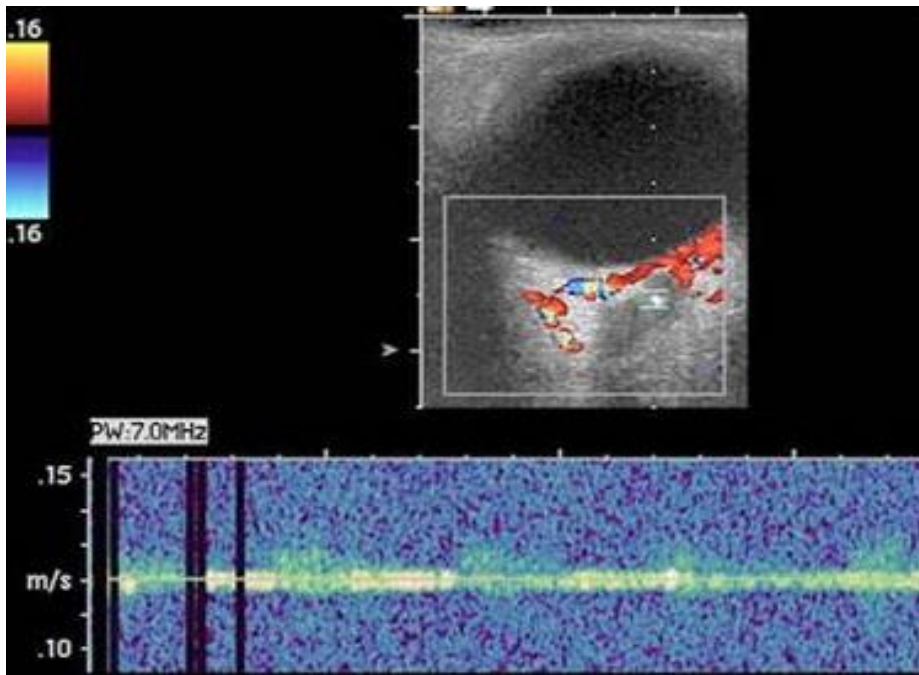


**THROMBOEMBOLIC
CRA OCCLUSION**

**Sensitivity 83%
Specificity 100%**

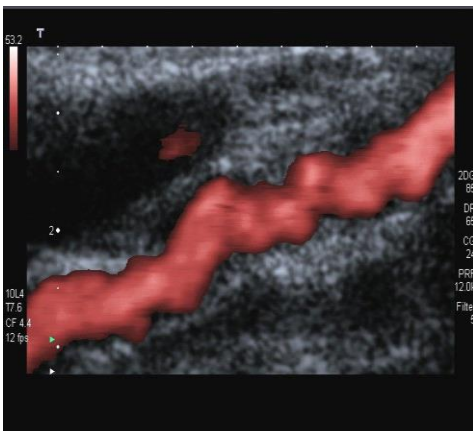


**detailed workup looking for
sources of emboli and
atherosclerosis**

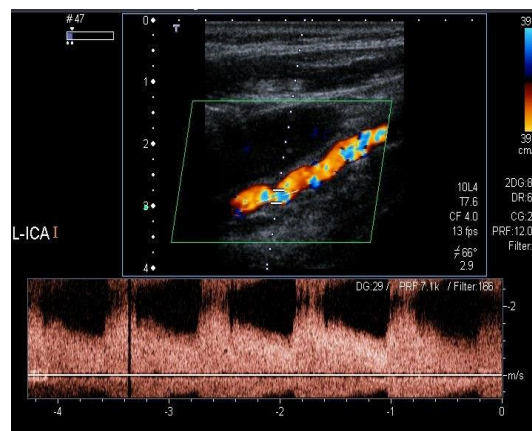


Fibromuscular dysplasia (FMD)

- Progressive segmental non-atherosclerotic and noninflammatory vasculopathy most commonly affects renal arteries and cervicocephalic arteries; ICA **proximal** C1 and C2 segment; asymptomatic in 90% of cases
- "String of pearls", tubular segment stenosis
- Methods of choice for Dg. are conventional angiography, MRA and CTA








String of pearls



segment stenosis

Genomics of Fibromuscular Dysplasia

Silvia Di Monaco^{1,2} , Adrien Georges³ , Jean-Philippe Lengelé^{1,4} , Miikka Vikkula⁵ 
and Alexandre Persu^{1,6,*} 

- ¹ Division of Cardiology, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, 1200 Brussels, Belgium; silvia.dimonaco@gmail.com (S.D.M.); Jean_Philippe.LENGELE@ghdc.be (J.-P.L.)
- ² Department of Medical Sciences, Internal Medicine and Hypertension Division, AOU Città della Salute e della Scienza, University of Turin, 10124 Turin, Italy
- ³ INSERM, UMR970 Paris Cardiovascular Research Center (PARCC), F-75015 Paris, France; adrien.georges@inserm.fr
- ⁴ Department of Nephrology, Grand Hôpital De Charleroi, 6060 Gilly, Belgium
- ⁵ Human Molecular Genetics, de Duve Institute, Université catholique de Louvain, 1200 Brussels, Belgium; miikka.vikkula@uclouvain.be
- ⁶ Pole of Cardiovascular Research, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, 1200 Brussels, Belgium
- * Correspondence: alexandre.persu@uclouvain.be; Tel.: +32-2-764-6306 or 32-2-764-2533; Fax: +32-2-764-8980

Received: 2 May 2018; Accepted: 16 May 2018; Published: 21 May 2018



Abstract: Fibromuscular Dysplasia (FMD) is “an idiopathic, segmental, non-atherosclerotic and non-inflammatory disease of the musculature of arterial walls, leading to stenosis of small and medium-sized arteries” (Persu, et al; 2014). FMD can lead to hypertension, arterial dissections, subarachnoid haemorrhage, stroke or mesenteric ischemia. The pathophysiology of the disease remains elusive. While familial cases are rare (<5%) in contemporary FMD registries, there is evidence in favour of the existence of multiple genetic factors involved in this vascular disease. Recent collaborative efforts allowed the identification of a first genetic locus associated with FMD. This intronic variant located in the phosphatase and actin regulator 1 gene (*PHACTR1*) may influence the transcription activity of the endothelin-1 gene (*EDN1*) located nearby on chromosome 6. Interestingly, the *PHACTR1* locus has also been involved in vascular hypertrophy in normal subjects, carotid dissection, migraine and coronary artery disease. National and international registries of FMD patients, with deep and harmonised phenotypic and genetic characterisation, are expected to be instrumental to improve our understanding of the genetic basis and pathophysiology of this intriguing vascular disease.

Keywords: fibromuscular dysplasia; non atherosclerotic vascular stenosis; *PHACTR1*; genetic association; cervical artery dissection; spontaneous coronary arteries dissection

Clinical Presentation

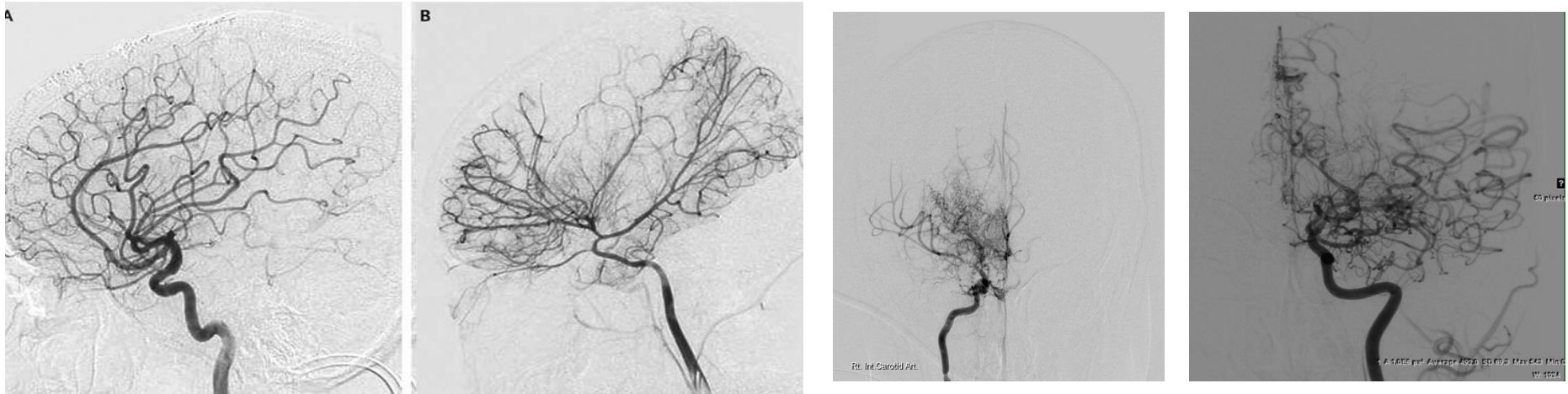
- Asymptomatic
- Nonspecific symptoms
 - Headaches, altered mentation, tinnitus, vertigo, carotidynia
- Neurologic symptoms
 - Transient ischemic attacks, cerebral infarctions, subarachnoid hemorrhages, syncope, Horner's syndrome, cranial nerve palsies

Arteries Involved	Frequency of Involvement (%)
Renal arteries	60–75
Bilateral	35
Extracranial cerebrovascular circulation (carotid or vertebral arteries)	25–30
Associated intracranial aneurysm	7–50
Multiple vascular beds	28
Other arterial beds (iliac, popliteal, splanchnic, hepatic, coronary, sub- clavian, brachial, aorta, superficial femoral, tibial, or peroneal)	Uncommon, exact frequency unknown

* Fibromuscular dysplasia may be a generalized process; in rare cases, it has also been identified in the venous system.

Moya-moya disease

- Progressive stenosis or occlusion of **terminal** portions of bilateral ICAs, proximal portions of ACA, MCA
- Rarely involves posterior circulation, including the basilar and posterior cerebral arteries.
- Compensatory formation of a fine vascular network (“puff of cigarette smoke”)



- Moyamoya disease: primary (idiopathic)
- Moyamoya syndrome: secondary moyamoya associated with a number of different putative causes

Clinical presentation

Symptoms

Frequent

Ischemic stroke

Transient ischemic attack

Headache

Occasional

Seizure

Choreiform movements

Intracranial Hemorrhage

(Common in adults uncommon in children)

Rare

Cognitive decline

Visual impairment

CLINICAL PICTURE

- **CHILDREN:** motor deficits, involuntary movements, headaches, dizziness, epileptic seizures; progressive mental retardation (> 50%);
- **ADULTS YELLOW RACE:** hemorrhage (ICH, SAH) from the rete mirabile, or aneurysms
- **ADULTS WHITE RACE:** cerebral ischemia

Diagnosis

- Clinical picture: younger patients with cerebrovascular disease without VRF
- MR: ICH in cortico-subcortical zones, basal ganglia, thalamus, subcortical, cortex, intraventricular bleeding
- MRA, angiography: 6 stages
- Angiographic criteria:
 1. Stenosis or occlusion of ICA, ACM or ACA terminal segments
 2. An abnormal vascular network of anastomosis near the stenosed or occluded arteries
 3. Bilateral changes
- 10% of aneurysm (Willis circle, smaller arteries: the front and rear choroidal arteries, rete mirabile)

Angiographic ICA staging system modified by Mugikura *et al.*

ICA stage	Angiographic findings
I	Mild to moderate stenosis around carotid bifurcation with absent or slightly developed ICA moyamoya: Almost the entire ACA and MCA branches are opacified in antegrade fashion
II	Severe stenosis around carotid bifurcation or occlusion of either of proximal ACA or MCA with well-developed ICA moyamoya: The ACA and/or MCA branches are clearly defective, but at least several of the ACA or MCA branches remain opacified in antegrade fashion
III	Occlusion of the proximal ACA and/or MCA with well-developed ICA moyamoya: Only a few of the ACA and/or MCA branches are faintly opacified in antegrade fashion through the meshwork of ICA moyamoya
IV	Complete occlusion of the proximal ACA and MCA with absent or small amount of ICA moyamoya: No opacification of either ACA or MCA branches in antegrade fashion

Treatment

The Japanese guidelines from 2012 recommend the use of anti-platelet aggregation drugs for the treatment of ischemic MMD, but the risk of bleeding remains.

Surgical revascularization of MMD includes 3 types: 1)direct revascularization, 2)indirect revascularization and 3)combined revascularization.

In the direct revascularization surgery, the most common method is superficial temporal artery-MCA anastomosis. When ischemic hypoperfusion occurs in the blood supply area of the ACA or posterior cerebral artery, the superficial temporal artery-ACA or occipital artery-posterior cerebral artery anastomosis may be adopted.

Indirect revascularization is a surgery based on a variety of tissues used as a source of blood supply, mainly including encephalomyosynangiosis.

A recent meta-analysis revealed that direct or combined revascularization surgery is better for unstable adult patients with MMD characterized by symptomatic or hemodynamic instability

FMD and / or MOYA MOYA?

	FMD	Moya moya
Population	White race, 25-75 years M: F = 1: 3-4	A yellow race, but not exclusively Children up to 5 years and adults 30-40 (60) years M: F = 1: 1.8
Ethiology	? ↓ Alfa1-antitrypsin? Inheritance?	? ↑ Base fibroblast growth factor (bFGF)
Localization	Extracranial carotid artery; media and intima	Intracranial terminal carotid artery; intima
Clinical picture	Often asymptomatic TIA, stroke	Children: deficits, retardation Adults: recurrent haemorrhage, white people - ischemia
Clinical course	Basically benign	Children have a serious clinical picture, adult relapse, but also up to 80% benign currents
Angiographic finding	"String of beads"	"Puff of smoke"
Therapy	Antiaggregation	ICA-ECA bypass



Think about non-atherosclerotic
vasculopathies in (young)
patients with stroke